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Masaharu Shigenobu\* Yoshihide Suzuki<sup>†</sup> Junichi Sato<sup>‡</sup>
Shoji Sadakane\*\* Naotoshi Maeda<sup>††</sup> Shunji Sano<sup>‡‡</sup>
Mitsuo Yamamoto<sup>§</sup> Hideki Kurahara Shigeru Teramoto Shigeru Teramoto

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<sup>\*</sup>Okayama University,

<sup>&</sup>lt;sup>†</sup>Okayama University,

<sup>&</sup>lt;sup>‡</sup>Okayama University,

<sup>\*\*</sup>Okayama University,

<sup>††</sup>Okayama University,

<sup>‡‡</sup>Okayama University,

<sup>§</sup>Okayama University,

<sup>¶</sup>Okayama University,

Okayama University,

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### **Abstract**

In the aortic stenosis group, the left ventricular (LV) muscle mass index was a good parameter for predicting the prognosis. Associated mitral valve disease had no influence on long term survival after aortic valve replacement. In the aortic insufficiency group, associated mitral valve disease had a marked influence on the results of aortic valve replacement. In general, the aortic insufficiency group had less clinical improvement postoperatively than the aortic stenosis group. In the annuloaortic ectasia group, left ventricular enddiastolic pressure (LVEDP) might be the predictor to the prognosis. This group had the worst prognosis, of the three groups. Early operation should be considered for patients who have no, or only mild symptoms of, aortic valve disease.

**KEYWORDS:** aortic valve replacement, late survival predictor, aoetic stenosis, aortic insufficiency, annuloaortic ectasia.

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## FACTORS INFLUENCING LONG-TERM SURVIVAL AFTER AORTIC VALVE REPLACEMENT

Masaharu Shigenobu, Yoshihide Suzuki, Junichi Sato, Shoji Sadakane, Naotoshi Maeda, Shunji Sano, Mitsuo Yamamoto, Hideki Kurihara and Shigeru Тегамото

The 2nd Department of Surgery, Okayama University Medical School,
Okayama 700, Japan
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Abstract. In the aortic stenosis group, the left ventricular (LV) muscle mass index was a good parameter for predicting the prognosis. Associated mitral valve disease had no influence on long term survival after aortic valve replacement. In the aortic insufficiency group, associated mitral valve disease had a marked influence on the results of aortic valve replacement. In general, the aortic insufficiency group had less clinical improvement postoperatively than the aortic stenosis group. In the annuloaortic ectasia group, left ventricular enddiastolic pressure (LVEDP) might be the predictor to the prognosis. This group had the worst prognosis, of the three groups. Early operation should be considered for patients who have no, or only mild symptoms of, aortic valve disease.

*Key words*: aortic valve replacement, late survival predictor, aortic stenosis, aortic insufficiency, annuloaortic ectasia.

The optimal time for aortic valve replacement (AVR) and the prognosis in patients with aortic valve diseases are difficult problems. Reports so far on predictors of the timing of AVR have been few and contradictory.

Clinical assessment, hemodynamic study, and quantitative angiographic measurement of the left ventricle may provide parameters for the prediction of survival after AVR. The purpose of the present study is to assess preoperative clinical, hemodynamic, and angiographic factors that might define perioperative and long-term survival following AVR.

#### MATERIALS AND METHODS

The records of 51 patients undergoing cardiac catheterization before aortic valve replacement between 1972 and 1978 were evaluated. Out of them, 34 patients (10 patients with aortic stenosis (AS), 16 patients with pure aortic insufficiency (AI) and 8 patients with annuloaortic ectasia (An)) had suitable data and are the basis of this study. The remaining 17 patients were excluded because quantitative angiographic data was not available.

Clinical, hemodynamic and quantitative angiographic variables were recorded from the medical chart or catheterization data as shown in Tables 1 and 2.

All patients underwent heart catheterization. Cardiac volume was measured

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by the method of Dodge (1). Peak systolic stress was determined by the formula of Timoshenko (2). Eccentricity ratio was measured by the method of Fischl (3). Left ventricular muscle mass was calculated by Rackley's method (4).

AVR was performed using cardiopulmonary bypass with mild hypothermia, moderate hemodilution, and left coronary artery perfusion in most cases. The Starr-Edwards model 2320 ball valve was used in 12 patients, Björk-Shiley valve was used in 13 patients and Lillehei-Kaster Valve was used in 9 patients. Anticoagulants were administered to all patients throughout the postoperative period.

Postoperative follow-up data were obtained from the records of hospitals and/or by interview of patients. We analysed the data precisely to identify the clinical, hemodynamic and angiographic variables that predicted the long-term survival in each group of AS, AI and An.

From these data, all patients were classified into two groups, that is, an improved group or an unimproved one. The improved group was defined as patients who achieved asymptomatic status or whose symptoms improved by at least two classes in the New York Heart Association (NYHA) classification. The unimproved group was defined as patients who were unimproved after AVR, or improved by only one class of the NYHA classification, or who died from cardiogenic causes.

#### RESULTS

Preoperative data. In the AS group, there was a significant difference in LV muscle mass index (P<0.05) and mean pulmonary arterial pressure (PAP) (P<0.05) between improved and unimproved patients. There was no significant difference in the other parameters  $(Table\ 1)$ .

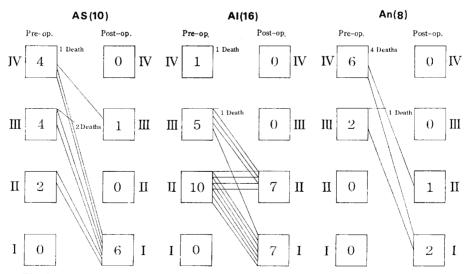


Fig. 1. The New York Heart Association (NYHA) functional class of 34 patients before and after aortic valve replacement. AS, Patients with aortic stenosis; AI, Patients with aortic insufficiency; An, Patients with annuloaortic ectasia. Number in parentheses indicates number of patients.

TABLE 1. COMPARISON BETWEEN THE IMPROVED AND THE UNIMPROVED GROUP IN EACH AORTIC VALVE DISEASE

ţ		AS	AS (10)	AI (16)	(16)	An	An (8)
Parameters		Improved group (6)	Unimproved group (4)	Improved group (7)	Unimproved group (9)	Improved group (3)	Unimproved group (5)
1 Age	(years old)	$34.0\pm 25.9$	43. $0 \pm 2.50$	33. $7 \pm 4.60$	43.6±4.87	$30.0\pm 2.63$	$35.8\pm3.34$
2 CTR	( % )	62. $7 \pm 1.95$	623 $\pm 4.67$	$58.9 \pm 1.36$	$59.3\pm 2.76$	71. $0\pm2.50$	67. $4\pm 0.25$
3 Period from onset of symptoms to operation	(mo.)	87. $0\pm 35.5$	59.8 $\pm$ 35.0	$52.1\!\pm\!25.2$	$63.6 \pm 14.3$	$8.67 \pm 3.61$	33. $4\pm14.6$
4 Operation time	(min)	412 $\pm 1.78$	$375 \pm 28.1$	$384 \pm 19.7$	$373 \pm 25.2$	$558 \pm 28.2$	$480 \pm 48.2$
5 Perfusion time	(min)	$142 \pm 5.86$	$145 \pm 11.5$	$109\ \pm 10.9$	$125 \pm 10.1$	195 $\pm 24.5$	184 $\pm 25.1$
6 SVI	$(ml/m^2)$	46.8 $\pm 2$ .55	34. $7 \pm 12.9$	$56.2 \pm 7.46$	$64.0\pm 8.66$	$65.3\pm 8.15$	$84.9 \pm 15.7$
7 EDVI	$(ml/m^2)$	$91.6\pm 6.57$	75. $3 \pm 6.15$	$169 \pm 18.4$	167 $\pm 22.4$	$163 \pm 55.3$	$209 \pm 33.1$
8 ESVI	$(\mathbf{ml/m}^2)$	$\textbf{44.8} \pm 5.84$	40. $6\pm 2.84$	$112\ \pm 17.5$	$103 \pm 15.3$	$97.5\pm50.6$	$124 \pm 24.8$
9 EF		$\textbf{0.}\ 52\pm0.\ 04$	$0.45\pm 0.06$	$0.34\pm0.04$	$0.40\pm0.03$	$0.50{\pm}0.12$	$0.41 \pm 0.06$
10 LV wall thickness	(cm)	1. $15 \pm 0.06$	1. $10 \pm 0.11$	$1.41\pm0.15$	$1.32\pm0.09$	$1.31\pm0.24$	$1.28\pm0.24$
11 LV muscle mass index	$(\mathbf{g}/\mathbf{m}^2)$	$109\ \pm 4.61$	$81.~0 \pm 10.~\mathbf{6*}$	178 $\pm 26.2$	180 $\pm$ 26.7	$187\ \pm 89.9$	$205 \pm 58.5$
12 Peak systolic stress	$(g/cm^2)$	$395 \pm 45.4$	$472 \pm 84.7$	$495 \pm 60.0$	443 $\pm$ 32. 4	$408 \pm 62.1$	$609 \pm 77.5$
13 Es		$0.88 \pm 0.02$	$0.88\pm0.01$	$0.86\pm0.01$	$0.85\pm0.02$	$0.79\pm0.02$	$0.69 \pm 0.05$
ED		$0.82\pm0.02$	$\textbf{0.81} \pm \textbf{0.02}$	0. $79 \pm 0.01$	0. $79\pm0.02$	$0.72\pm0.02$	$0.60\pm0.05$
14 mean PAP	(mmHg)	$24.5\pm1.35$	18.8 $\pm$ 0.96*	$1.\ 71\pm4.\ 00$	23. $4 \pm 5$ . 05	19. $3\pm 5$ . 95	$32.6 \pm 3.35$
15 LVEDP	(mmHg)	10.8 $\pm$ 1.76	10.5 $\pm$ 2.78	$11.1 \pm 1.97$	$14.9\pm 1.99$	12. $7\pm 1.44$	$26.2\pm4.37*$

(X±S.E.) \*P<0.05 AS, Aortic stenosis; AI, Aortic insufficiency; An, Annuloaortic ectasia, CTR: Cardiothoracic ratio, SVI: Stroke volume index, EDVI: Enddiastolic volume index, ESVI: Endsystolic volume index, EF: ejection fraction, Es: Eccentricity ratio at endsystole, ED: Eccentricity ratio at enddiastole, PAP: Pulmonary arterial pressure, LVEDP: Left ventricular enddiastolic pressure, mo: month, min: minutes. Number in parentheses indicates number of patients. 192

Four patients of the AS group belonged to Class IV of the NYHA classification, four patients were Class III and 2 patients were Class II (Fig. 1).

In the AI group, there were no significant differences in any parameters between improved and unimproved patients (Table 1). One of the 16 patients was classified as Class IV of the NYHA classification. Five were Class III, and ten were Class II (Fig. 1).

In the An group, there was a significant difference in LVEDP (P < 0.05) but no difference in the other parameters (Table 1). Clinically, six were Class IV, and the other 2 patients were Class III of the NYHA classification (Fig. 1). In the An group, 7 were complications of Marfan's syndrome and the other patient suffered from the aortitis syndrome (Table 2).

Postoperative data. In the AS group, one of the Class IV patients died from the low cardiac output syndrome on the 16th postoperative day. Two of them had excellent improvement to Class I. The remaining patient had only minimal improvement. Two of the Class III patients died from congestive heart failure, on the 45th postoperative day and five months after AVR. Two patients in Class II preoperatively improved to Class I (Table 2). In the AI group, 2 patients died from left heart failure, one was Class IV and the other one was Class III preoperatively. One of the Class III patients had clinical improvement to Class I, three improved by only one class, and four had no clinical improvement. The remaining 6 patients of the Class II group improved to Class I (Table 2).

TABLE 2. CLINICAL DATA OF EACH GROUP (AS, AI AND An)

Age	Sex	Sex Diagnosis		NYHA class		ΓR	Surgical procedure	Follow-up Period	Outcome
Ų	-			a	b a procedure	renou			
Aor	tic s	tenosis					:		
31	M	AS+MS	I	l	61	53	AVR(S-E#9) MC	4 yr. 10 mo.	Doing well
26	M	AS		l	55	55	AVR (B-S#21)	4 yr. 2 mo.	Doing well
34	F	AS+MS	M	I	62	59	AVR (B-S#23) MC	4 yr.	Doing well
30	F	AS + MS	IV	I	65	55	AVR (B-S#21) MC	3 yr. 7 mo.	Doing well
37	M	AS	I	I	62	51	$AVR(B-S\sharp 21)$	3 yr. 7 mo.	Doing well
46	F	AS+MS	IV	I	71	65	AVR (L-K#16) MC	2 yr.	Doing well
36	F	AS .		_	60	_	$AVR(S-E\sharp 10)$	death	Died from CHF on 45th POD
44	M	AS	H	_	54	_	AVR (S-E#10)	death	Died from CHF 5 mo. after surgery
42	M	AS+MS	IV	I	57	60	AVR (B-S#21) MC	3 yr. 5 mo.	On digitalis & diuretics
50	F	AS + MS	IV		78	·	AVR(L-K♯16) MC	death	Died from LOS on 16th POD

Table 2 continued

### Late Survival Predictor in Aortic Valve Replacement

Table 2 continued

Age	Sex	Diagnosis		/HA lass	C	TR	Surgical procedure	Follow-up period	Outcome
			b	a	b	a	procedure	period	. 9
Aorti	c ins	uficiency							
20	M	AI	1	I	59	49	AVR (S-E#10)	6 yr. 9 mo.	Doing well
18	F	AI	I	I	60	50	AVR (S-E#9)	5 yr. 2 mo.	Doing well
23	M	AI	1	I	56	49	AVR (S-E#9)	4 yr. 2 mo.	Doing well
41	F	AI	I	I	63	57	AVR(B-S#21)	4 yr. 2 mo.	Doing well
40	M	AI	I	I	52	48	AVR (B-S#21)	$2  \mathrm{yr.}  9  \mathrm{mo.}$	Doing well
52	M	AI	M	I	59	52	AVR (B-S#23)	l yr. 11 mo.	Doing well
42	M	AI	I	I	63	65	AVR(L-K#18)	1 yr. 7 mo.	Doing well
67	M	AI + MS	I	I	50	45	AVR (S-E#10) MC	4 yr. 10 mo.	On diuretics
36	F	AI+MS	ĮV		63		AVR(S-E#9) MC	Death	Died from CHF 4yr, after surger
33	M	AI + MS	1	I	60	57	AVR (B-S#23) MC	3 yr. 2 mo.	On digitalis
26	F	AI + MR	Ш	ı	73	70	AVR (B-S#21) MAP	3 yr. 2 mo.	On diuretics & digitalis
50	M	AI + MR	I	_	60		AVR (B-S#23) MAP	death	Died from LOS on 5th POD
20	M	AI + MS	I	I	47	50	AVR (L-K#16) MG	1 yr. 9 mo.	On digitalis
53	M	AI+MS	II	1	56	60	AVR(L-K#16) MC	1 yr. 7 mo.	On digitalis
55	M	AI	l	I	71	65	AVR (L-K#16)	1 yr.	On diuretics
52	M	AI	I	I	54	52	AVR (L-K#16)	10 mo.	On diuretics & digitalis
Annul	oaor	tic ectasia						137 6	3 7 7 M
25	M	Marfan	IV	I	65	52	AVR (S-E#14) grafting	6 yr. 9 mo.	Doing well
29	F	Aortitis	H	I	75	59	AVR (S-E#14) grafting	6 yr.1 mo.	Doing well
36	F	Marfan	IV	I	73	57	Bentall(L-K#18)	7 mo.	Doing well
29	M	Marfan	IV		71		AVR (S-E#14) grafting	Death	Died suddenly 5 yrs. after surge
32	F	Marfan	<b>IV</b>	_	56	-	AVR(S-E#11) grafting	Death at	Died on table
39	M	Marfan	IV		79		Bentall(B-S#29)	Death	Died suddenly 3 yrs. after surge
30	F	Marfan	<b>IV</b>		73		Bentall (B-S#29)	Death	Died on table
49	M	Marfan	I	_	58	_	AVR(L-K#18) grafting	Death	Died from CHF on 11th POD

NYHA: New York Heart Association, MS: Mitral stenosis, MR: Mitral regurgitation, S-E: Starr-Edwards, B-S: Björk-Shiley, L-K: Lillehei-Kaster, MC: Mitral commissurotomy, MAP: Mitral annuloplasty, CHF: Congestive heart failure. POD: Postoperative day, LOS: Low output syndrome. Other abbreviations are the same as those in Table 1.

The An group had 5 deaths, that is, 2 of the Class IV patients died suddenly, 3 years and 5 years after surgery. Two of the Class IV patients died during operation. One of the Class III group died from congestive heart failure. The rest of this group had excellent clinical improvement (Table 2).

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#### DISCUSSION

Determining the optimal time for AVR is the most difficult decision, especially for patients with aortic valve disease who are asymptomatic. Valve replacement is commonly undertaken for relief of symptoms. Other indications include relief of critical stenosis, control of infective endcarditis, prolongation of life and preservation of left ventricular function.

Usually, clinical findings were used to determine the optimal operation time, or to predict the time when the left ventricle suffered irreversible impairment. Frank et al. (5), in previous studies on the natural history of isolated aortic stenosis, reported a three year mortality of 36%, 52% at five years, and 90% at 10 years. The onset of left ventricular failure generally has been considered to be a grave prognostic sign in patients with AS; moreover, previous studies suggest that the onset of syncope carries a poor prognosis, even if the duration of the syncopal periods varies considerably.

In aortic incompetence, Spagnuolo et al. (6) found that the triad of marked radiographic evidence of LV enlargement, wide pulse pressure and electrocardiographic diagnosis of ventricular hypertrophy identified patients at high risk for the development of congestive heart failure, angina, or death.

However, these clinical data are of limited assistance in asymptomatic or mildly symptomatic patients with AS or AI who exhibit some clinical features. There have been some studies (7–9) on parameters for predicting the prognosis after AVR, but most group include all kinds of aortic valve diseases together for study. We emphasize that the three kinds of aortic valve disease (AS, AI and An) should be analysed independently, because we suspect that each aortic valve disease has its own indices related to prognosis and the optimal operation time. In our study, for instance, a significant difference between AS and AI was evident in some parameters (the period from the onset of symptoms to operation, perfusion time, stroke volume index (SVI), enddiastolic volume index (EDVI), endsystolic volume index (ESVI), ejection fraction (EF) and LV muscle mass index) even before operation.

In the AS group, there was a significant difference in the LV muscle mass index and the mean pulmonary arterial pressure between the improved group and the unimproved group. The improved group had a higher value for the LV muscle mass index than the unimproved group. In AS, the left ventricle of the improved group can compensate for the chronic pressure load by hypertrophy in order to normalize wall stress and overcome the elevated afterload. As a result, LV systolic pump function remains normal. The unimproved group, however, does not have enough LV hypertrophy to compensate for the chronic pressure load, so it may show less clinical improvement after surgery. For this reason, the LV muscle mass index is a good parameter for predicting the prognosis in AS.

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The improved group showed higher mean pulmonary arterial pressure than the unimproved group. More cases are needed to identify the cause in detail. There was no significant difference in other parameters in the AS group, possibly because patients with AS maintained good left ventricular function even in late stages of the disease.

In AS, deaths were confined to the Class III or IV patients of the NYHA classification. Duvoisin et al. (10) reported that patients in Class III or IV showed low suvival rates after AVR in both the short and long term. Eight of 10 cases had angina before surgery (the frequent symptoms in AS), although there was no relation between symptoms and prognosis. Six patients had mitral commissurotomy for mild or moderate degrees of mitral stenosis. One died from congestive heart failure. Other patients had marked improvement to Class I. Therefore, association of mitral stenosis, even mild or moderate, had no direct effect on the prognosis.

In the AI group, there was no significant difference in any parameters between the improved group and the unimproved group. Seven of 9 patients, who were not improved after AVR, had associated mitral valve diseases (mitral regurgitation or mitral stenosis). On the other hand, 7 of 9 patients with isolated AI and no mitral valve disease had remarkable clinical improvement postoperatively. Therefore, the association of mitral valve disease apparently has a marked effect on the prognosis in the AI group.

In contrast to chronic AI, acute AI has a volume load placed suddenly on the left ventricle, which results in an increase in wall tension. The left ventricle, dilated by the sudden increase in volume without compensatory hypertrophy, has much greater systolic stress upon its wall and falls rapidly into left ventricular failure. These patients should be treated as candidates for emergency surgery.

In the An group, Murdoch (11) reported that the average age of 72 cases who died was 32 years old, and that the causes of death were mostly cardiogenic. LVEDP might be a good parameter for predicting the prognosis, because, in our study, the unimproved group had significantly higher values of LVEDP than the improved group. In general, annuloaortic ectasia has the worst prognosis. Nasrallah (12) reported a 5 year mortality rate of 57% in 30 patients who underwent surgery. Most patients died suddenly from acute dissection after operation.

The An group are mostly candidates for operation, but the prognosis is poor because of the basic disease.

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